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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,249	12/17/2001	Manuel Vega	37851-911	7196

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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,249	VEGA ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *30 and 31* is/are allowed.

6)☒ Claim(s) *1-29,32,33 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments, filed February 1, 2006, have been fully considered and they are to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. However, in light of the amendments, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, 2nd Paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-29, 32, 33, and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 22, 23, 24, and 27 were amended to include the limitation of "the host cells are provided as an addressable array." This limitation is unclear since it seems to state that the cells themselves are an addressable array, rather than the cells are found in an addressable array or the cells are organized in an addressable array. Clarification via clearer language is requested.

Claim 10 is unclear because it refers back to step (d) of claim 9, but claim 9 has no step (d). Furthermore, there is no step (d) in claim 1 that recites a set of nucleic acid molecules.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-21, 27, 32, 33, 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zlauddin et al. (Nature (May 2001) Volume 411, pages 107-110) in view of Short (US 6,171,820).

The instant claims are drawn to a method identifying a protein with particular characteristics by introducing nucleic acids into a cell microarray, where in each microarray location, the introduced nucleic acids are the same, expressing the encoded proteins from each location, and screening the proteins for a particular property.

Regarding claims 1, 9 and 27, Zlauddin et al. teach a method the produces a set of nucleic acid molecules that encode for the same protein (page 107, right column – page 108, left column, top paragraph); individually introducing each set of nucleic acid molecules to the cells (page 107, right column – page 108, left column, top paragraph; Figure 1 and text); where the host cells are on an addressable array and the cells of each locus have the same nucleic acid molecule (page 107, right column – page 108, left column, top paragraph; Figure 1 and text); expressing the encoded protein (page 108, left column); and screening the proteins for a chemical or biological property (page 108, left column).

However Zlauddin et al. do not use their method for nucleic acid molecules that encode modified forms of a target protein, or designate a protein as a hit, or that each hit contains a mutation designated a hit position.

Short discloses a method of producing a set of mutagenized progeny polynucleotides encoding a polypeptide from a parental template polynucleotide (i.e. target protein), via "codon site-saturation mutagenesis" wherein at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids (Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51) and the identification of protein mutational positions (i.e. hit position) (Column 4, line 64 to Column 5, line 34; and Column 12, lines 20-24).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Zlauddin et al. and Short to gain the benefit of

screening for proteins using live cells. Zlauddin et al. list several advantages of their method, which includes accelerating the pace of expression cloning and allowing for screens using a variety of detection methods (page 109, left column, bottom paragraph – right column). Zlauddin et al. teach a generic method that may be used with any cDNA constructs. Furthermore, Zlauddin et al. teach that their cell microarrays can be stored longer that protein microarrays for protein studies (page 109, right column). Such protein studies would include identifying novel proteins of a desired property. Short et al. teach a similar method of transfecting host cells with cDNA constructs on an array (Column 11, lines 38-46; Column 20, lines 51-58., and Columns 55-56, beginning on line 34). Also similarly to Zlauddin et al., Short teaches that the purpose of his invention is to identify proteins of a desired property (column 4, lines 55-64). It would have been obvious to one of ordinary skill in the art to use the mutagenized progeny polynucleotides of Short in Zlauddin et al.'s method to create microarray of cells expressing mutagenzied polynucleotides. Thus one of ordinary skill in the art would be motivated to combine the methods of Zlauddin et al. and Short to gain the benefit of creating a microarray that accelerates the pace of expression cloning, allows for a variety of detection methods, has increased storage life to identify proteins of a desired property.

Regarding claims 2 and 10, Short teaches wherein each set of nucleic acid molecules are individually designed and synthesized (Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51).

Regarding claims 3, 5, 6, 8, Zlauddin et al. teach wherein each set is deposited at a locus in an array that comprises a solid support with wells (page 107, right column – page 108, left column, top paragraph; Figure 1 and text); wherein the nucleic acid molecules comprise plasmids and the cells are bacterial cells (Column 11, lines 38-46; Column 20, lines 51-58., and Columns 55-56, beginning on line 34)

Regarding claims 4 and 7, Short teaches wherein each polynucleotide in a set encodes a protein that differs from at least one amino acid from the target protein (Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51); wherein the nucleic acid molecules comprise viral vectors and the cells are transduced with the vectors (page 107, right column – page 108, left column, top paragraph; Figure 1 and text; page 109, right column, 2nd paragraph from the bottom).

Regarding claims 11, 12, 13-15, 19, and 42-44, Short teaches producing nucleic acid molecules by site-directed mutagenesis (Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51); producing nucleic acid molecules by changing each codon in a target to a pre-selected group wherein the proteins in each set differ from the proteins in another set by one amino acid (codon mutatagenesis (N,N,G/T), (Figure 2; Column 6, lines 47-60).

Regarding claim 16-18, Short discloses producing nucleic acid molecules by replacing each codon is a position, with another codon encoding another amino acid, (Column 11, lines 38-46; Column 20, lines 51-58., and Columns 55-56, beginning on line 34; Column 5, lines 8-11); recombining the nucleic acid molecules, introducing them into cells and screening the cells (Column 11, lines 38-46; Column 20, lines 51-58., and

Columns 55-56, beginning on line 34; Column 5, lines 8-11); and recombining two, three, or more of the nucleic acids encoding the leads (Column 11, lines 38-46; Column 20, lines 51-58., and Columns 55-56, beginning on line 34; Column 5, lines 8-11).

Regarding claim 20 and 21, Short discloses wherein the modifications are effected in the selected domain of the target protein or the full length of the target protein (Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51).

Regarding claims 32 and 33, According to the MPEP Section 2106, Part VI, "merely using a computer to automate a known process does not by itself impart nonobviousness to the invention. *See Dann v. Johnston, 425 U.S. 219, 227-30, 189 USPQ 257, 261 (1976); In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).*" Claims 32 and 33 are merely computer automations of claim 1. Thus, it would be obvious to one skilled in the art to use a computer to automate the known processes disclosed by Zlauddin et al. and Short.

6. Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zlauddin et al. (Nature (May 2001) Volume 411, pages 107-110) in view of Short (US 6,171,820) further in view of Collett et al. (US 2002/0081574 B1).

The instant claims are drawn to a method identifying a protein with particular characteristics by introducing nucleic acids into a cell microarray, where in each microarray location, the introduced nucleic acids are the same, expressing the encoded

proteins from each location, and screening the proteins with a change in activity of the target of at least 10-50% compared to the unmodified target protein.

Zlauddin et al. and Short are applied as above.

Zlauddin et al. and Short do not explicitly teach wherein the change in activity of the target proteins is at least 10-1000% compared to an unmodified target protein.

Collett et al. teaches screening modified proteins with a 10-25 fold change in activity (page 6, paragraph 49, Table 1; Figure 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Zlauddin et al., Short, and Collett et al. to gain the benefit of determining the activity of protein for finding useful proteins. See above for the motivation to combine Zlauddin et al. with Short. Zlauddin et al. and Short state that the purpose of their invention is study protein properties, in particular for high throughput screening methods. Both Zlauddin et al. and Short's objective is to find useful proteins. Collett et al. teach a method that helps determine if a protein is useful by measuring their activity (page 6, paragraph 49, Table 1; Figure 3). Also it is noted that determining the enzymatic activity is well known in the art at the time of the invention. In order to determine if a protein was useful or not, one of ordinary skill in the art would be motivated to also determine the activity of the protein. Thus one of ordinary skill in the art would have been motivated to combine the references of Zlauddin et al., Short, and Collett et al.

7. Claims 24 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zlauddin et al. (Nature (May 2001) Volume 411, pages 107-110) in view of Short (US 6,171,820) further in view of Berlioz et al. (US 5,925,565).

The instant claims are drawn to a method identifying a protein with particular characteristics by introducing viral nucleic acids into a cell microarray, where in each microarray location, the introduced viral nucleic acids are the same, assessing the titer of the viral vectors, expressing the encoded proteins from each location, and screening the proteins for a particular property.

Zlauddin et al. and Short are applied as above.

Zlauddin et al. and Short do not explicitly teach assessing the titer of the viral vectors in each set of cells.

Berlioz et al. teaches assessing the titer of the viral vectors after transfection for each set of cells (column 14, lines 39-65).

Short et al. teaches targeting proteins involved in viral replications (column 19, lines 30-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Zlauddin et al., Berlioz et al., and Short in order to gain the advantage of determining the stability and efficiency of the vectors. Berlioz et al. state that one of his goals is to create the efficient and stable expression of genes (column 1, lines 10-17). Part of their method requires that they assess the titer of the viral vectors after transmission. Both Short and Zlauddin et al. rely heavily on using vectors to transfect their cells which causes the cells to express a protein. In using

Short and Zlauddin et al.'s method, one of ordinary skill in the art would want to know if the vectors are properly transfecting the cells and the cells are properly expressing the desired protein. Thus one of ordinary skill in the art would use the method of Berlioz to determine if the cells are properly being transfected when using Short and Zaluddin et al.

Allowable Subject Matter

8. Claims 30 and 31 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

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